UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

25/JUN/2014

MEMORANDUM: Acute Toxicity Data Evaluation Record (DER) for UPI Glufosinate Technical

Subject:	Name of Pesticide Product:	UPI Glufosinate Technical
	EPA File Symbol:	70506-GNT
	DP Barcode:	D415524
	Decision No.:	482599
	Action Code:	R333
	PC Codes:	128850 Glufosinate

From: Tracy Keigwin, Biologist
Technical Review Branch
Registration Division (7505P)

M Harlin - TOXICOLOGY

To: Grant Rowland, RM Team 23
Herbicide Branch
Registration Division (7505P)

Applicant: United Phosphorus, Inc.
630 Freedom Business Center
King of Prussia, PA 19406

FORMULATION FROM LABEL*:

Active Ingredient(s):	% by wt.
Glufosinate-ammonium	97.0
Other Ingredient(s):	3.2
Total:	100.0%

***Incorrect ingredient statement – label must be revised to reflect the correct concentrations.**

ACTION REQUESTED: The Risk Manager requests a review of acute toxicity studies submitted in support of EPA File Symbol 70506-GNT, UPI Glufosinate Technical.

BACKGROUND: United Phosphorus, Inc. has submitted an application for the registration of EPA File Symbol 70506-GNT, UPI Glufosinate Technical. In support of their application the registrant has submitted the following acute toxicity studies: MRID Nos. 49205715 (870.1100), 49205716 (870.1200), 49205717 (870.1300), 49205718 (870.2400), 49205719 (870.2500) and 49205720 (870.2600). The product label states that UPI Glufosinate Technical is for use only in formulation of herbicides.

GLP: All studies were conducted in accordance with GLP.

DEFICIENCIES/DEVIATIONS: The primary eye irritation study (MRID 49205718) is unacceptable. The acute oral toxicity study (MRID 4925715) is supplementary, but may be used for regulatory purposes. Please see item #1 (below) in the "Comments and Recommendations" section for complete details.

COMMENTS AND RECOMMENDATIONS:
1) Only 4 of the 6 acute toxicity studies are acceptable.

The primary eye irritation study (MRID 49205718) is **Unacceptable**. The study states that "...At 1 hour post (test item application), eyes of all the rabbits were gently washed with 0.9% normal saline to remove any residual test item... (Page 14)". HED Test Guidelines 870.2400 state that "the eyes of the test animals should not be washed out for 24 hours following instillation of the test substance." This study is considered unacceptable and is not upgradeable. A new primary eye irritation study must be submitted or cited before this product can be registered.

The acute oral toxicity study (MRID 49205715) is classified as **Supplementary**. The AOT 425 Stat Program states that an incorrect dosing sequence was used. Although the study classifies the acute oral LD_{50} as 1514 mg/kg this cannot be assumed. As no deaths were observed at the 1090 mg/kg dose level the LD_{50} for this product must be classified as being greater than 1090 mg/kg bw.

At present, the acute toxicity profile for EPA File Symbol 84229-GNT is as follows:

acute oral toxicity	III	**Supplementary**	MRID 49205715
acute dermal toxicity	III	Acceptable	MRID 49205716
acute inhalation toxicity	IV	Acceptable	MRID 49205717
primary eye irritation*	-	**Unacceptable**	MRID 49205718
primary skin irritation	IV	Acceptable	MRID 49205719
dermal sensitization	NO	Acceptable	MRID 49205720

*Primary eye irritation study is **unacceptable** and is not upgradable. The acute oral toxicity study is supplementary, but may be used for regulatory purposes.

2) The Basic CSF (dated August 28, 2013) must be approved by the product chemistry team before this action can be finalized.

3) The precautionary and first aid statements for this product will be provided once an acceptable primary eye irritation study has been submitted or cited.

Reviewer: Tracy Keigwin **Date:** June 25, 2014
Risk Manager (EPA): 23

The following table is the Acute Toxicity Data Evaluation Record (DER) for the six studies submitted for the proposed product, EPA File Symbol 70506-GNT:

1. DP BARCODE: 415524				
2. PC CODES: 128850				
3. CURRENT DATE: June 25, 2014				
4. TEST MATERIAL: Glufosinate Ammonium Technical (Batch number UPH-11/GF-331/15; Purity: 96.81 (%w/w) Glufosinate Ammonium; white colored powder)				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute oral toxicity / rat Jai Research Foundation (Gujarat, India) JRF Study Number 401-1-01-6540/ July 4, 2013 OCSPP 870.1100; OECD 425	49205715	LD_{50} Females > 1090 mg/kg bw At 1090 mg/kg (3 rats) all survived. No clinical symptoms observed at this dose level. No gross abnormalities observed at necropsy. At the 1750 mg/kg bw all rats (2/2) died within 2 days of dosing. Prior to death animals exhibited lethargy. At necropsy, decedents exhibited congestion of the lungs or liver. **This study is supplementary.** Per AOT 425 Stat Program an incorrect dosing sequence was used. Although the study states that the LD_{50} is 1514 mg/kg bw, due to the incorrect dosing sequence TRB determines the LD_{50} is greater than 1090 mg/kg bw. This study may still be used for regulatory purposes since an acute oral toxicity category can still be determined.	III	S
Acute dermal toxicity / rat Jai Research Foundation (Gujarat, India) JRF Study Number 403-1-01-6541/ June 17, 2013 OCSPP 870.1200; OECD 402	49205716	LD_{50} > 2000 mg/kg bw (both sexes and combined). No mortality observed in the control group (distilled water application; 5 males and 5 females) or test group (2000	III	A

		mg/kg test substance application; 5 males and 5 females). No signs of toxicity, dermal irritation or abnormal behavior observed in either group. No gross abnormalities observed at necropsy.		
Acute inhalation toxicity / rat Jai Research Foundation (Gujarat, India) JRF Study Number 405-1-01-6542/ July 11, 2013 OCSPP 870.1300; OECD 403	49205717	LC_{50} > 2.164 mg/L (Nose-only, gravimetric; both sexes and combined). The MMAD and GSD were 2.87 µm and 2.92, respectively. All rats survived. A decrease in bodyweight was observed in on day 1 in males and on study day 1 and 3 in females; however all animals exceeded their initial bodyweight by study termination (day 14). No other clinical abnormalities observed. No gross abnormalities observed at necropsy.	IV	A
Primary eye irritation / rabbit Jai Research Foundation (Gujarat, India) JRF Study Number 407-1-01-6544/ July 4, 2013 OCSPP 870.2400; OECD 405	49205718	No corneal opacity, iritis or conjunctivitis observed. MMTS = 0.0. **<u>This study is unacceptable and is not upgradable</u>**. The eyes of test animals were washed at one hour post-instillation, which is unacceptable per HED Test Guidelines 870.2400. .	-	**U**
Primary dermal irritation / rabbit Jai Research Foundation (Gujarat, India) JRF Study Number 406-1-01-6543/ July 5, 2013 OCSPP 870.2500; OECD 404	49205719	PDII = 0.25 (slightly irritating). Grade 1 erythema was observed at test sites in all animals (3/3) at the one hour observation only. No erythema or edema was observed in the control sites at any time. All scores were zero by the 24 hour observation. Note that the study incorrectly states that the PDII is 0.0. The	IV	A

		correct PDII is 0.25 (slightly irritating)		
Dermal sensitization / Guinea pig Jai Research Foundation (Gujarat, India) JRF Study Number 408-1-01-6019/ April 15, 2013 OCSPP 870.2600; OECD 406	49205720	Not a sensitizer. Tested using Magnusson-Kligman maximization method. 10 test animals and 5 controls. Induction intradermal injection (control) – a) 1:1 mixture (v/v) FCA with distilled water; b) distilled water; c) 1:1 (v/v) mixture of injection a) and injection b). Induction intradermal injection (test) – a) 1:1 mixture (v/v) FCA with distilled water; b) 5.0% (v/v) glufosinate-ammonium technical in distilled water; c) 1:1 (v/v) mixture of injection a) and injection b). Induction Topical (Note that 0.5mL 10% (w/v) sodium laurel sulfate in vaseline was applied to test area to augment skin irritation) – 100 mg glufosinate- ammonium technical moistened with 0.2 mL distilled water. Control animals received 0.2mL distilled water on patch and placed on control site. Challenge dose – 0.2 mL of test substance at 100 mg glufosinate-ammonium technical moistened with 0.2 mL applied to a patch and placed on the test site. Following challenge, no positive dermal irritation was observed in either the 5 control or 10 test animals at 24 or 48 hours. The results of a positive control using α-Hexylcinnamaldehyde were appropriate (JRF study # 408-1-01-5816; 05/FEB/2013).	NO	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, D = Data Gap